UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/632,711	08/01/2003	Dennis A. Carson	02307O-124010US	2786

20350 7590 11/01/2005

TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
GRAFFEO, MICHEL	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 11/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/632,711	CARSON ET AL.	
	Examiner	Art Unit	
	Michel Graffeo	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,14-17,21-26,35-38 and 51-58* is/are pending in the application.

4a) Of the above claim(s) *9-13,18-20,27-34,39-50 and 59-62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,14-17,21-26,35-38 and 51-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/25/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Action

In response to the Restriction/Election mailed on August 24, 2005, Applicant has elected with traverse Group I, claims 1-8, 14-17, 21-26, 35-38 and 51-58 in the Response to Restriction Requirement date September 26, 2005.

Claims 1-8, 14-17, 21-26, 35-38 and 51-58 are pending and examined and claims 9-13, 18-20, 27-34, 39-50 and 59-62 have been withdrawn.

Applicant's election with traverse of Group I in the reply filed on September 26, 205 is acknowledged. The traversal is on the ground(s) that the required IMPDH inhibitor and agent that inhibits a cellular process regulated by GTP or ATP of Group I are also found in Group II and further that the examination of both Group I and Group II. This is not found persuasive because a search of the compound is not coextensive with a search of the method.

The requirement is still deemed proper and is therefore made FINAL.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. No application shall be entitled to the benefit of an earlier filed provisional application under 35 U.S.C. 119(e) unless an amendment containing the specific reference to the earlier filed provisional application is submitted at such time during the pendency of the application as required by the Director. Applicant has not complied with one or more conditions for receiving

the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows: no reference to the earlier filed provisional application is made in the Specification. Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 5,358,855 to Markovic et al. in view of US Patent No. 5,405,837 to Weber, further in view of Chen et al. Evaluation of mizoribine as an immunosuppressant in subrenal capsule assay using immunocompetent mice. Japanese Journal of Cancer Research: Gann, (1990 Feb)81 (2) 183-7 and further in view of Leoni et al. Indanocine,

a Microtubule-Binding Indanone and a Selective Inducer of Apoptosis in Multidrug-Resistant Cancer Cells. Journal of the National Cancer Institute, Vol. 92, No.3 (2000).

Markovic et al. teach specifically that IMPDH inhibitors, such as tiazofurin and mycophenolic acid, have been used as cancer chemotherapeutic treatments (in current claims 1,3; see col 1 lines 19-28).

Markovic et al. do not specifically teach the use of mizoribine for example together with an α-tubulin polymerization inhibitor such as indanocine.

Weber teaches the treatment of cancer comprising tiazofurin in concert with a second component (in current claims 1-8; see col 2 lines 6-14) such as ribavirin (another chemotherapeutic agent).

Chen et al. teach that mizoribine, a IMPDH inhibitor (see page 186 second column), effectively reduces the size of tumors (in current claims 1-8; see Fig. 2 on page 185).

Leoni et al. teach that indanocine has antiproliferative activity (in current claim 5; see especially Background) in for example, breast cancer (in current claims 6-8; see Discussion on page 222).

One of ordinary skill in the art would have been motivated to combine the above references and as combined would teach the invention as claimed. One of ordinary skill in the art would have been motivated to combine the above references primarily because Weber teaches that tiazofurin, an IMPDH inhibitor, should be used in conjunction with another agent. Moreover, all four references are directed to chemotherapeutic agents (Chen et al. and Leoni et al. cited to show the knowledge of

mizoribine and indanocine in the art) and combining agents which are known to be useful as chemotherapeutics individually into a single composition useful for the very same purpose is *prima facie* obvious. See In re Kerkhoven 205 USPQ 1069. Since it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose, the idea of combining an IMPDH inhibitor and an α-tubulin polymerization inhibitor flows logically from their having been individually taught in the prior art. Thus, the combined references teach and make prima facie obvious how to use the claimed invention at the time that it was made.

Claims 14-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 5,358,855 to Markovic et al. in view of US Patent No. 5,405,837 to Weber, further in view of Chen et al. Evaluation of mizoribine as an immunosuppressant in subrenal capsule assay using immunocompetent mice. Japanese Journal of Cancer Research: Gann, (1990 Feb)81 (2) 183-7 and further in view of Uckun et al. Biology and Treatment of Childhood T-Lineage Acute Lymphoblastic Leukemia. Blood, (91);, 1998. 735-746.

Markovic et al. teach specifically that IMPDH inhibitors, such as tiazofurin and mycophenolic acid, have been used as cancer chemotherapeutic treatments (in current claims 14-17; see col 1 lines 19-28).

Markovic et al. do not specifically teach the use of mizoribine for example together with a precursor of Ara-GTP such as guanine arabinoside (Ara-G).

Weber teaches the treatment of cancer comprising tiazofurin in concert with a second component (in current claims 14-17; see col 2 lines 6-14) such as ribavirin (another chemotherapeutic agent).

Chen et al. teach that mizoribine, a IMPDH inhibitor (see page 186 second column), effectively reduces the size of tumors (in current claims 14-18; see Fig. 2 on page 185).

Uckun et al. teach that Ara-G is selectively cytotoxic for T-cell lines and T-lineage leukemic cells (in current claims 14-18; see page 741 bottom if first column).

One of ordinary skill in the art would have been motivated to combine the above references and as combined would teach the invention as claimed. One of ordinary skill in the art would have been motivated to combine the above references primarily because Weber teaches that tiazofurin, an IMPDH inhibitor, should be used in conjunction with another agent. Moreover, all four references are directed to chemotherapeutic agents (Chen et al. and Uckun et al. cited to show the knowledge of mizoribine and Ara-G in the art) and combining agents which are known to be useful as chemotherapeutics individually into a single composition useful for the very same purpose is *prima facie* obvious. See In re Kerkhoven 205 USPQ 1069. Since it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose, the idea of combining an IMPDH inhibitor and a precursor of Ara-GTP flows logically from their having been individually taught in the prior art. Thus, the

combined references teach and make prima facie obvious how to use the claimed invention at the time that it was made.

Claims 21-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 5,358,855 to Markovic et al. in view of US Patent No. 5,405,837 to Weber, further in view of Chen et al. Evaluation of mizoribine as an immunosuppressant in subrenal capsule assay using immunocompetent mice. Japanese Journal of Cancer Research: Gann, (1990 Feb)81 (2) 183-7 and further in view of US Patent No. 5,840,505 to Carrerra et al.

Markovic et al. teach specifically that IMPDH inhibitors, such as tiazofurin and mycophenolic acid, have been used as cancer chemotherapeutic treatments (in current claims 21-26; see col 1 lines 19-28).

Markovic et al. do not specifically teach the use of mizoribine for example together with an inhibitor of the de novo pathway of purine biosynthesis such as l-alanosine.

Weber teaches the treatment of cancer comprising tiazofurin in concert with a second component (in current claims 21-26; see col 2 lines 6-14) such as ribavirin (another chemotherapeutic agent).

Chen et al. teach that mizoribine, a IMPDH inhibitor (see page 186 second column), effectively reduces the size of tumors (in current claims 21-26; see Fig. 2 on page 185).

Carrerra et al. teach a method of treating cancer, for example cancer cells that are deficient in MTAP activity (in current claim 26; see Abstract), with L-alanosine (in current claims 21-26; see col 1 lines12-20).

One of ordinary skill in the art would have been motivated to combine the above references and as combined would teach the invention as claimed. One of ordinary skill in the art would have been motivated to combine the above references primarily because Weber teaches that tiazofurin, an IMPDH inhibitor, should be used in conjunction with another agent. Moreover, all four references are directed to chemotherapeutic agents (Chen et al. and Carrerra et al. cited to show the knowledge of mizoribine and inhibitors of de novo purine biosynthesis) and combining agents which are known to be useful as chemotherapeutics individually into a single composition useful for the very same purpose is *prima facie* obvious. See In re Kerkhoven 205 USPQ 1069. Since it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose, the idea of combining an IMPDH inhibitor and inhibitors of de novo purine biosynthesis flows logically from their having been individually taught in the prior art. Thus, the combined references teach and make prima facie obvious how to use the claimed invention at the time that it was made.

Claims 35-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 5,358,855 to Markovic et al. in view of US Patent No. 5,405,837 to Weber, further in view of Chen et al. Evaluation of mizoribine as an immunosuppressant

in subrenal capsule assay using immunocompetent mice. Japanese Journal of Cancer Research: Gann, (1990 Feb)81 (2) 183-7 and further in view of US Patent Application No. 2003/0003057 to Weers et al.

Markovic et al. teach specifically that IMPDH inhibitors, such as tiazofurin and mycophenolic acid, have been used as cancer chemotherapeutic treatments (in current claims 35-38; see col 1 lines 19-28).

Markovic et al. do not specifically teach the use of mizoribine for example together with a GPCR antagonist such as leuprolide.

Weber teaches the treatment of cancer comprising tiazofurin in concert with a second component (in current claims 35-38; see col 2 lines 6-14) such as ribavirin (another chemotherapeutic agent).

Chen et al. teach that mizoribine, a IMPDH inhibitor (see page 186 second column), effectively reduces the size of tumors (in current claims 35-38; see Fig. 2 on page 185).

Weers et al. teach a method of treating cancer comprising leuprolide, a GPCR antagonist (in current claims 35-38; see Abstract).

One of ordinary skill in the art would have been motivated to combine the above references and as combined would teach the invention as claimed. One of ordinary skill in the art would have been motivated to combine the above references primarily because Weber teaches that tiazofurin, an IMPDH inhibitor, should be used in conjunction with another agent. Moreover, all four references are directed to chemotherapeutic agents (Chen et al. and Weers et al. cited to show the knowledge of

mizoribine and leuprolide) and combining agents which are known to be useful as chemotherapeutics individually into a single composition useful for the very same purpose is *prima facie* obvious. See In re Kerkhoven 205 USPQ 1069. Since it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose, the idea of combining an IMPDH inhibitor and leuprolide flows logically from their having been individually taught in the prior art. Thus, the combined references teach and make prima facie obvious how to use the claimed invention at the time that it was made.

Claims 51-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 5,358,855 to Markovic et al. in view of US Patent No. 5,405,837 to Weber, and further in view of Chen et al. Evaluation of mizoribine as an immunosuppressant in subrenal capsule assay using immunocompetent mice. Japanese Journal of Cancer Research: Gann, (1990 Feb)81 (2) 183-7.

Markovic et al. teach specifically that IMPDH inhibitors, such as tiazofurin and mycophenolic acid, have been used as cancer chemotherapeutic treatments (in current claims 51-58; see col 1 lines 19-28).

Markovic et al. do not specifically teach the use of mizoribine in any particular amounts.

Weber teaches the treatment of cancer comprising tiazofurin in concert with a second component (in current claims 51-58; see col 2 lines 6-14) such as ribavirin

(another chemotherapeutic agent). Moreover, Weber teaches various modes of administration (injection, infusion etc.) and dosing regimes (in current claims 51-58; see col 3 lines 32-36) greater than 4,400mg/m^2 (see col 4 lines25-27) or in a range between 1100-3300 mg/m^2 (see col 4 lines 25-28 and 44-45). Although Weber does not specifically recite administration via oral mode or parenteral, one of ordinary skill in the art would find it obvious to do so, absent evidence to the contrary. Also, absent evidence to the contrary is the teaching of such a broad range of dosing regimes for tiazofurin that one of ordinary skill in the art would appreciate and find obvious the routine optimization of dosing amounts and routes of administration for comparable IMPDH inhibitor, mizoribine, to meet the limitations of the instant claims.

Chen et al. teach that mizoribine, a IMPDH inhibitor (see page 186 second column), effectively reduces the size of tumors (in current claims 51-58; see Fig. 2 on page 185).

One of ordinary skill in the art would have been motivated to combine the above references and as combined would teach the invention as claimed. One of ordinary skill in the art would have been motivated to combine the above references primarily because Weber teaches that tiazofurin, an IMPDH inhibitor, is an effective chemotherapeutic agent. Moreover, all three references are directed to chemotherapeutic agents (Chen et al. cited to show the knowledge of mizoribine) and Markovic et al. teaching effectiveness of other IMPDH inhibitors such as tiazofurn. Thus, the combined references teach and make prima facie obvious how to use the claimed invention at the time that it was made.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michel Graffeo whose telephone number is 571-272-8505. The examiner can normally be reached on 9am to 5:30pm Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

24 October 2005
MG

***

M6

DWAYNE JONES
PRIMARY EXAMINER